

**REMARKS**

Entry of the foregoing amendments and reconsideration of the subject application as amended pursuant to and consistent with 37 C.F.R. § 1.111, in light of the remarks which follow, is respectfully requested.

**1. Status of the Claims**

Upon entry of the foregoing amendment, claims 1-16 are pending in the application.

Claim 3 is newly amended herein. Claim 3 has been amended to further clarify the invention as suggested by the Examiner.

Claims 15 and 16 are newly added. Support for claims 15 and 16 is found, for example, in original claim 3, and, elsewhere throughout the specification.

The amendments are not believed to add new matter and entry is respectfully requested.

**2. Objections to the Claims**

At page 2 of the Office Action, the Office objects to claim 3, stating “[t]he two terms in parentheses should be deleted and included in a dependent claim.” In reply thereto, claim 3 has been amended. The deleted subject matter has been placed into new claims 15 and 16 as suggested by the Examiner.

Accordingly, the objection to claim 3 has been overcome. Reconsideration and withdrawal of the objection is respectfully requested.

**3. Claim Rejection under 35 U.S.C. § 103(a)**

At page 2 of the Office Action, the Office rejects claims 1-4, 9 and 10 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Azizi et al. (Azizi et al., *PNAS* 95(7): 3908-3913 (March 1998)) in view of Kohyama et al. (Kohyama et al., *Differentiation* 68(4-5): 235-244, Abstract only (October 2001)). Claim 3 is newly amended. Claims 5-8 and 11-14 are objected to as dependent upon a rejected claim. The rejection is respectfully traversed.

At the outset, it is noted that the publication date of Kohyama is later (October 2001) than the priority date of the instant application (May 1999). Therefore, Kohyama can not be a prior

art reference to anticipate, or render obvious, the pending claims because the priority date of the present application predates the publication date of Kohyama. **Kohyama cannot qualify as prior art to the instant claims under any circumstance (i.e., under 35 U.S.C. § 102(b) or 35 U.S.C. § 103).** A reading of the file indicates the Office has been notified once before (*see*, Amendment and Reply, page 9, dated November 223, 2004) that Kohyama does not qualify as available prior art for a rejection under 35 U.S.C. § 102(b) in view of the earlier filing date of the priority document. If the Office maintains the Kohyama reference as a prior art reference of the rejection, the Office is respectfully requested to provide an explanation of why Kohyama is proper prior art against the instant claims.

The Office argues Azizi discloses transplantation of human marrow stromal cells and astrocyte precursors (neurospheres); that transplanted cells behave like endogenous CNS stem cells; and, that, allegedly, Azizi provides the suggestion to use the implants in the treatment of various CNS diseases. The Office states Azizi differs from the claims in that Azizi does not teach that transplanted cells would differentiate into parenchymal cells. The Office relies on Kohyama for the disclosure that bone marrow stromal cells differentiate into functional neurons.

The Office concludes the claimed methods would have been obvious, arguing that those of ordinary skill would expect similar therapeutic results for treatment of various CNS diseases given that Azizi discloses the direct implantation of human marrow stromal cells and Kohyama's teaching that the transplanted cells would differentiate into functional neurons. However, Kohyama, having a later publication date than the claimed priority date, cannot be applied against the pending claims for reasons discussed, above. Having removed Kohyama as a prior art reference, Azizi remains as the sole reference allegedly rendering obvious the pending claims.

As the Office is aware, the burden of establishing a case of *prima facie* obviousness rests with the Patent and Trademark Office. *In re Fine*, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988). Moreover, an obviousness rejection "must be based on *evidence* (statutory prior art, admissions against interest)...." *In re McKellin*, 188 U.S.P.Q. 428, 432 (C.C.P.A. 1976), emphasis in original.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to

combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991). The Office *prima facie* case fails on all three criteria for the following reasons.

Azizi fails to teach the transplanted cells would differentiate into parenchymal cells as is claimed (*i.e.*, claims 1 and 4); and, Azizi fails to use a diseased or damaged brain (*i.e.*, claims 1-4). No where does Azizi administer, or suggest the administration of, the cells into brains of rats that have been subjected to conditions that would amount to a diseased or damaged state such as a brain injury, a spinal cord injury or a neurodegenerative disease. At best, Azizi teaches survival, engraftment, and migration of marrow stromal cells following transplantation into brains of normal, healthy rats, and broadly speculates that the cells can be used to treat diseases of the central nervous system (Abstract). Thus, Azizi fails to fulfill the first criterion, the suggestion or motivation to modify the reference to meet the elements of the claims.

Upon reading Azizi, the skilled artisan is given no reasons to believe that administering the cells to a patient in need would be a successful treatment of a disease. The skilled artisan is provided with no more than a mere suggestion based on speculation that diseases of the central nervous system can be treated using bone marrow stromal cells. While the skill in the medical biotechnology arts is high, it is not so elevated that the skilled artisan can reasonably expect to obtain a successful treatment of a patient suffering from a brain or spinal cord injury or neurodegenerative disease from the teachings of Azizi (*see*, Amendment of 11/23/04, at 8). Azizi does not provide the "reasonable expectation of success," the second criterion, required for a proper *prima facie* case of obviousness.

Finally, Azizi, failing to teach or suggest all the elements of the claims, fails to fulfill the third criterion of a proper *prima facie* case. Specifically, as discussed above and as acknowledged by the Office (Office Action at 3), Azizi fails to teach the transplanted cells would differentiate into parenchymal cells as is claimed; and, Azizi fails to use a diseased or damaged brain, also as claimed.

The Office *prima facie* case of obviousness fails to meet any of the criteria for a proper *prima facie* case and is therefore legally deficient. Accordingly, Azizi fails to render obvious any of the pending claims.

In view of the arguments above and amendments to the claims, claims 1-14 are allowable. The rejection is believed nonapplicable to new claims 15 and 16, dependent from now allowable claim 3.

Reconsideration and withdrawal of the rejection of claims 1-4, 9 and 10 under 35 U.S.C. § 103(a) is respectfully requested.

### **CONCLUSION**

In conclusion, this amendment and reply is believed to be a full response to the outstanding Office Action. Should any issues remain outstanding or if there are any questions concerning this paper, or the application in general, the Examiner is invited to telephone the undersigned representative at the Examiner's earliest convenience.

**EXCEPT** for issue fees payable under 37 C.F.R. § 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. §§ 1.16 and 1.17 which may be required, including any required extension of time fees, and Notice of Appeal fees, or credit any overpayment to Deposit Account No. 50-0573. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F.R. § 1.136(a)(3).

Respectfully submitted,

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Enclosures: -petition for three months  
extension of time;  
-accompanying fee to extend  
time for response to and through July 31, 2006